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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S.

Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESS: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Model Cell Lines With and Without AKT1 Mutations Derived from Proteus Syndrome Patients

Description of Technology: The Proteus syndrome is a congenital disorder characterized by patchy overgrowth and hyperplasia (cell proliferation) of multiple tissues and organs, along with susceptibility to developing tumors. It is a rare disorder, with incidence of less than one case per million, caused by a somatic mutation. It is also a mosaic disorder, that is one in which cells of the same person have different genetic content from one another. The NHGRI inventors have generated cell lines from patients with Proteus syndrome and discovered that a somatic activating mutation in the serine-threonine kinase AKT1 is associated with Proteus syndrome. AKT1 is an oncogene and an enzyme known to mediate cell proliferation and apoptosis (programmed cell death process) and has been a target for anti-cancer therapies. A number of single-cell lines with the AKT1 mutation showing increased AKT1 phosphorylation and their matched controls without the mutation have been generated. The cell lines can be used to screen therapeutic targets for AKT1, for study design, as models of Proteus syndrome and early stages of cancerous conditions.

Potential Commercial Applications:

- Cell lines generated from patients with Proteus syndrome
- Obtained a number of single-cell lines with the AKT1 mutation and their matched controls without the mutation
- Cell lines with the mutation showed increased AKT1 phosphorylation for activating mutation

Competitive Advantages:

- Screening of potential therapeutics that target AKT1
- Cell lines have well-matched controls for rigorous study design
- Serves as model cell lines of Proteus syndrome and early stages of cancerous

conditions

Development Stage:

- Prototype
- Clinical
- In vivo data available (human)

Inventors: Leslie G. Biesecker and Marjorie J. Lindhurst (NHGRI)

Publication: Lindhurst MJ, et al. A mosaic activating mutation in AKT1 associated with the Proteus syndrome. N Engl J Med. 2011 Aug 18;365(7):611-619. [PMID 21793738]

Intellectual Property: HHS Reference No. E-033-2012/0 — Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Whitney Hastings, Ph.D.; 301-451-7337;
hastingw@mail.nih.gov

Non-toxic Compounds that Inhibit the Formation and Spreading of Tumors

Description of Technology: Available for licensing are novel pyrrolopyrimidine compounds that disrupt the assembly of the perinucleolar compartment (PNC), a sub-nuclear structure highly prevalent in metastatic tumors. These notable compounds act without overt cytotoxicity.

The presence of the PNC positively correlates with metastatic capacity, making it a potential marker for cancer development and prognosis. These compounds could also serve as useful tools to elucidate the biology driving the formation and maintenance of the PNC, and unravel its association with metastasis.

Potential Commercial Applications:

- Use in the therapeutic intervention of metastasis in cancer
- Use as tools to elucidate the biology of the PNC

Competitive Advantages:

- No existing FDA-approved treatment for the clinical management of metastasis
- Target is specific to metastatic tumors
- Compounds are not toxic
- Broadly acting across all metastatic cancers

Development Stage:

- Early-stage
- In vitro data available

Inventors: Samarjit Patnaik et al. (NCATS)

Intellectual Property: HHS Reference No. E-276-2011/0 — U.S. Provisional Application No. 61/576,780 filed 16 Dec 2011

Licensing Contact: Patrick McCue, Ph.D.; 301-435-5560;

mccuepat@mail.nih.gov

Collaborative Research Opportunity: The National Center for Advancing Translational Sciences is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this

technology. For collaboration opportunities, please contact Lili M. Portilla, MPA at 301-217-2589 or Lilip@nih.gov.

Novel Radio-labeled Agents for Imaging Alzheimer's Disease-associated Amyloid

Description of Technology: This technology introduces novel radio-labeled agents for imaging amyloid deposits in the brains of Alzheimer's Disease patients. These are small molecule, radio-ligand compounds that are analogs of benzo[d]thiazole. They are highly specific to amyloid, have low background noise, do not undergo rapid defluoridation and do not produce residual radioactivity in the brain. In addition, the compounds are stable and may be readily synthesized from commercially available starting materials. These compounds may be used in many noninvasive imaging techniques including: magnetic resonance spectroscopy (MRS) or imaging (MRI), or positron emission tomography (PET) or single-photon emission computed tomography (SPECT) to measure amyloid. Non-invasive detection of Alzheimer's disease-associated amyloid plaques in the brain would be valuable for early diagnosis, monitoring, and for clinical development of therapeutic drugs.

Potential Commercial Applications: Imaging agents for use in magnetic resonance spectroscopy (MRS), or imaging (MRI), positron emission tomography (PET) or single -photon emission computed tomography (SPECT).

Competitive Advantages: Highly specificity to amyloid, low background, do not undergo rapid defluoridation and do not produce residual radioactivity in the brain.

Development Stage: Early-stage

Inventors: Lisheng Cai and Victor W. Pike (NIMH)

Publications:

1. Cai L, et al. Synthesis and structure-affinity relationships of new 4-(6-iodo-H-imidazo[1,2-a]pyridin-2-yl)-N-dimethylbenzeneamine derivatives as ligands for human beta-amyloid plaques. J Med Chem. 2007 Sep 20;50(19):4746-4758. [PMID 17722900]
2. Cai L, et al. Synthesis and evaluation of N-methyl and S-methyl ¹¹C-labeled 6-methylthio-2-(4'-N,N-dimethylamino)phenylimidazo[1,2-a]pyridines as radioligands for imaging beta-amyloid plaques in Alzheimer's disease. J Med Chem. 2008 Jan 10;51(1):148-158. [PMID 18078311]

Intellectual Property: HHS Reference No. E-225-2011/0 — U.S. Provisional Application No. 61/535,569 filed 16 Sep 2011

Related Technology: HHS Reference No. E-156-2006/0 — U.S. Patent Application No. 12/293,340 filed 17 Sep 2008

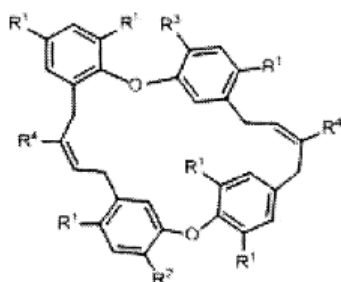
Licensing Contact: Tedd Fenn, J.D.; 301-435-5031; Tedd.Fenn@nih.gov

Collaborative Research Opportunity: The National Institute of Mental Health (NIMH) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Beta-amyloid Imaging Agents. For collaboration opportunities, please contact Suzanne L. Winfield, Ph.D. at winfiels@intr.nimh.nih.gov or 301-402-4324.

A New Class of Broad-spectrum Antibiotics: Naturally-occurring Chrysophaetins and Their Analogues

Description of Technology: This invention, offered for licensing and commercial development, relates to a new class of naturally occurring antimicrobial compounds called Chrysophaetins, and to their synthetic analogues. Isolated from an alga species, the mechanism of action of these compounds is through the inhibition of bacterial cytoskeletal protein FtsZ, an enzyme necessary for the replication of bacteria. FtsZ is responsible for Z-ring assembly in bacteria, which leads to bacterial cell division. Highly conserved among all bacteria, FtsZ is a very attractive antimicrobial target.

The chrysophaetin exhibits antimicrobial activity against drug resistant bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecalis* (VRE), as well as other drug susceptible strains. The general structure of the natural compound is shown below:



Potential Commercial Applications:

- Therapeutic potential for treating general and drug-resistant bacterial infections in clinical and veterinary populations.
- Antiseptics in hospital settings.

Competitive Advantages:

- Effective for commonly occurring drug-resistant infections MRSA and VRE.

- Broad spectrum of efficacy because mechanism of action is against the bacterial protein FtsZ, which has similar structure in all bacteria.

- Potential for additive efficacy when combined with other antibiotics due to distinct mechanism of action.

- Other drugs with similar structure and antibacterial properties can be synthesized using the chemical structure template shown above.

Development Stage:

- Early-stage
- In vitro data available

Inventors: Carole A Bewley, et al. (NIDDK)

Publication: Plaza A, et al. Chrysophaentins A-H, antibacterial bisdiarylbutene macrocycles that inhibit the bacterial cell division protein FtsZ. J Am Chem Soc. 2010 Jul 7;132(26):9069-9077. [PMID 20536175]

Intellectual Property: HHS Reference No. E-116-2010/0 — PCT Application No. PCT/US2011/026200 filed 25 Feb 2011, which published as WO 2011/106630 on 01 Sep 2011

Licensing Contact: John Stansberry, Ph.D.; 301-435-5236;
stansbej@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Bioorganic Chemistry, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the chrysophaentin antibiotics. Please

contact Marguerite J. Miller at 301-451-3636 or millermarg@niddk.nih.gov for more information.

February 21, 2012
Date

Richard U. Rodriguez,
Director
Division of Technology Development and Transfer
Office of Technology Transfer
National Institutes of Health

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